

quence Range: 1 to 6200

10 20 30 40 50 60 70  
\* \* \* \* \*  
GACGGATCGG GAGATCTCCC GATCCCCCTAT GGTCTGACTCT CAGTACAATC TGCTCTGATG CCGCATAGTT  
80 90 100 110 120 130 140  
\* \* \* \* \*  
AAGCCAGTAT CTGCTCCCTG CTTGTGTGTT GGAGGTCGCT GAGTAGTGCG CGAGCAAAAT TTAAGCTACA  
150 160 170 180 190 200 210  
\* \* \* \* \*  
ACAAGGCAAG GCTTGACCGA CAATTGCATG AAGAATCTGC TTAGGGTTAG GCGTTTTGCG CTGCTTCGCG  
220 230 240 250 260 270 280  
\* \* \* \* \*  
ATGTACGGGC CAGATATACG CGTTGACATT GATTATTGAC TAGTTATTAA TAGTAATCAA TTACGGGGTC  
290 300 310 320 330 340 350  
\* \* \* \* \*  
ATTAGTTCAT AGCCCATATA TGGAGTTCCG CGTTACATAA CTTACGGTAA ATGGCCCGCC TGGCTGACCG  
360 370 380 390 400 410 420  
\* \* \* \* \*  
CCCAACGACC CCCGCCATT GACGTCAATA ATGACGTATG TTCCCATAGT AACGCCAATA GGGACTTTCC  
430 440 450 460 470 480 490  
\* \* \* \* \*  
ATTGACGTCA ATGGGTGGAC TATTTACGGT AAAC TGCCCCA CTTGGCAGTA CATCAAGTGT ATCATATGCC  
500 510 520 530 540 550 560  
\* \* \* \* \*  
AAGTACGCCC CCTATTGACG TCAATGACGG TAAATGGCCC GCCTGGCATT ATGCCCAGTA CATGACCTTA  
570 580 590 600 610 620 630  
\* \* \* \* \*  
TGGGACTTTC CTACTTGGCA GTACATCTAC GTATTAGTCA TCGCTATTAC CATGGTGATG CGGTTTTTGGC  
640 650 660 670 680 690 700  
\* \* \* \* \*  
AGTACATCAA TGGGCGTGGA TAGCGGTTTG ACTCACGGGG ATTTCCAAGT CTCCACCCCA TTGACGTCAA  
710 720 730 740 750 760 770  
\* \* \* \* \*  
TGGGAGTTTG TTTTGGCACC AAAATCAACG GGACTTTCCA AAATGTCGTA ACAACTCCGC CCCATTGACG  
780 790 800 810 820 830 840  
\* \* \* \* \*  
CAAATGGGCG GTAGGCGTGT ACGGTGGGAG GTCTATATAA GCAGAGCTCT CTGGCTAACT AGAGAACCCA  
850 860 870 880 890 900 910  
\* \* \* \* \*  
CTGCTTAACT GGCTTATCGA AATTAATACG ACTCACTATA GGGAGACCCA AGCTTCGCAG AATTCCTGCG  
920 930 940 950 960 970 980  
\* \* \* \* \*  
GCTGCTACAG TGTGTCCAGC GTCCTGCCTG GCTGTGCTGA GUGCTGGAAC AGTGGCGCAT CATTCAAGTG  
990 1000 1010 1020 1030 1040 1050  
\* \* \* \* \*  
CACAGTTACC CATCCTGAGT CTGGCACCTT AACTGGCACA ATTGCCAAAG TCACAGGTGA GCTCAGATGC

09993241.111301

FIGURE 1

099341-11301

no gaps

|  |            |  |            |            |            |            |
|--|------------|--|------------|------------|------------|------------|
| 1060   | 1070       | 1080   | 1090       | 1100       | 1110       | 1120       |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      | * * *      |
| ATACCAGGAC   | ATTGTATGAC | GTTCCCTGCT   | CACATGCCTG | CTTCTTCCT  | ATAATACAGA | TGCTCAACTA |
| 1130   | 1140       | 1150   | 1160       | 1170       | 1180       | 1190       |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      | * * *      |
| ACTGCTCATG   | TCCTTATATC | ACAGAGGGAA   | ATTGGAGCTA | TCTGAGGAAC | TGCCCAGAAG | GGAAGGGCAG |
| 1200   | 1210       | 1220   | 1230       | 1240       | 1250       | 1260       |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      | * * *      |
| AGGGGTCTTG   | CTCTCCTTGT | CTGAGCCATA   | ACTCTTCTTT | CTACCTTCCA | GTGAACACCT | TCCCACCCCA |
| 1270   | 1280       | 1290   | 1300       | 1310       | 1320       | 1330       |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      | * * *      |
| GGTCCACCTG   | CTACCGCCGC | CGTCGGAGGA   | GCTGGCCCTG | AATGAGCTCT | TGTCCCTGAC | ATGCCTGGTG |
| 1340   | 1350       | 1360   | 1370       | 1380       | 1390       | 1400       |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      | * * *      |
| CGAGCTTTCA   | ACCCTAAAGA | AGTGCTGGTG   | CGATGGCTGC | ATGGAAATGA | GGAGCTGTCC | CCAGAAAGCT |
| 1410   | 1420       | 1430   | 1440       | 1450       | 1460       | 1470       |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      | * * *      |
| ACCTAGTGTT   | TGAGCCCCTA | AAGGAGCCAG   | GCGAGGGAGC | CACCACCTAC | CTGGTGACAA | GEGTGTTCG  |
| 1480   | 1490       | 1500   | 1510       | 1520       | 1530       | 1540       |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      | * * *      |
| TGTATCAGCT   | GAAAGCTTGA | TATCGAATTC   | CGGAGGCGGA | ACCGGCAGTG | CAGCCCGAAG | CCCCGCAGTC |
| 1550   | 1560       | 1570   | 1580       | 1590       |            |            |
| * * *  | * * *      | * * *  | * * *      | * * *      |            |            |
| CCCCGAGCACG  | CGTGGCC    | ATG CGT CCC CTG CGC CCC CGC GCC GCG CTG CTG GCG CTC CTG  |            |            |            |            |
|  |            | Met Arg Pro Leu Arg Pro Arg Ala Ala Leu Leu Ala Leu Leu> |            |            |            |            |
|  |            | a a a a a a ORF RF[1] a a a a a a>                       |            |            |            |            |
| 1600   | 1610       | 1620   | 1630       | 1640       | 1650       |            |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      |            |
| GCC TCG CTC CTG GCC GCG CCC CCG GTG GCC CCG GCC GAG GCC CCG CAC CTG GTG CAT  |            |  |            |            |            |            |
| Ala Ser Leu Leu Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro His Leu Val His> |            |  |            |            |            |            |
| a a a a a a a a ORF RF[1] a a a a a a a a>                                   |            |  |            |            |            |            |
| 1660   | 1670       | 1680   | 1690       | 1700       | 1710       |            |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      |            |
| GTG GAC GCG GCC CGC GCG CTG TGG CCC CTG CGG CGC TTC TGG AGG AGC ACA GGC TTC  |            |  |            |            |            |            |
| Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe> |            |  |            |            |            |            |
| a a a a a a a a ORF RF[1] a a a a a a a a>                                   |            |  |            |            |            |            |
| 1720   | 1730       | 1740   | 1750       | 1760       | 1770       |            |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      |            |
| TGC CCC CCG CTG CCA CAC AGC CAG GCT GAC CAG TAC GTC CTC AGC TGG GAC CAG CAG  |            |  |            |            |            |            |
| Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln> |            |  |            |            |            |            |
| a a a a a a a a ORF RF[1] a a a a a a a a>                                   |            |  |            |            |            |            |
| 1780   | 1790       | 1800   | 1810       | 1820       |            |            |
| * * *  | * * *      | * * *  | * * *      | * * *      |            |            |
| CTC AAC CTC GCC TAT GTG GGC GCC GTC CCT CAC CGC GGC ATC AAG CAG GTC CGG ACC  |            |  |            |            |            |            |
| Leu Asn Leu Ala Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg Thr> |            |  |            |            |            |            |
| a a a a a a a a ORF RF[1] a a a a a a a a>                                   |            |  |            |            |            |            |
| 1830   | 1840       | 1850   | 1860       | 1870       | 1880       |            |
| * * *  | * * *      | * * *  | * * *      | * * *      | * * *      |            |
| CAC TGG CTG CTG GAG CTT GTC ACC ACC AGG GGG TCC ACT GGA CGG GGC CTG AGC TAC  |            |  |            |            |            |            |
| His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr> |            |  |            |            |            |            |

103 (seq id)

FIGURE 1A







AAAAAAAAA AAAAAAAAAAG AATTCCTGCA GCCCGGGGGA TCCACTAGTT CTAGAGGGCC CGTTTAAACC

3760 3770 3780 3790 3800 3810 3820  
\* \* \* \* \*  
CGCTGATCAG CCTCGACTGT GCCTTCTAGT TGCCAGCCAT CTGTTGTTTG CCCCTCCCCC GTGCCTTCCT

3830 3840 3850 3860 3870 3880 3890  
\* \* \* \* \*  
TGACCCTGGA AGGTGCCACT CCCACTGTCC TTTCCTAATA AATGAGGAA ATTGCATCGC ATTGTCTGAG

3900 3910 3920 3930 3940 3950 3960  
\* \* \* \* \*  
TAGGTGTCAT TCTATTCTGG GGGGTGGGGT GGGGCAGGAC AGCAAGGGGG AGGATTGGGA AGACAATAGC

3970 3980 3990 4000 4010 4020 4030  
\* \* \* \* \*  
AGGCATGCTG GGGATGCGGT GGGCTCTATG GCTTCTGAGG CGGAAAGAAC CAGCTGGGGC TCGAGAGCTT

4040 4050 4060 4070 4080 4090 4100  
\* \* \* \* \*  
GGCGTAATCA TGGTCATAGC TGTTTCCTGT GTGAAATTGT TATCCGCTCA CAATTCCACA CAACATACGA

4110 4120 4130 4140 4150 4160 4170  
\* \* \* \* \*  
GCCGGAAGCA TAAAGTGTA AGCCTGGGGT GCCTAATGAG TGAGCTAACT CACATTAATT GCGTTGCGCT

4180 4190 4200 4210 4220 4230 4240  
\* \* \* \* \*  
CACTGCCCCG TTTCCAGTCG GGAAACCTGT CGTGCCAGCT GCATTAATGA ATCGGCCAAC GCGCGGGGAG

4250 4260 4270 4280 4290 4300 4310  
\* \* \* \* \*  
AGGCGGTTTG CGTATTGGGC GCTCTTCCGC TTCCTCGCTC ACTGACTCGC TGCCTCGGT CGTTCGGCTG

4320 4330 4340 4350 4360 4370 4380  
\* \* \* \* \*  
CGGCGAGCGG TATCAGCTCA CTCAAAGGCG GTAATACGGT TATCCACAGA ATCAGGGGAT AACGCAGGAA

4390 4400 4410 4420 4430 4440 4450  
\* \* \* \* \*  
AGAACATGTG AGCAAAAGGC CAGCAAAAGG CCAGGAACCG TAAAAAGGCC GCGTTGCTGG CGTTTTTCCA

4460 4470 4480 4490 4500 4510 4520  
\* \* \* \* \*  
TAGGCTCCGC CCCCCTGACG AGCATCACAA AAATCGACGC TCAAGTCAGA GGTGGCGAAA CCCGACAGGA

4530 4540 4550 4560 4570 4580 4590  
\* \* \* \* \*  
CTATAAAGAT ACCAGGCGTT TCCCCCTGGA AGCTCCCTCG TGCCTCTCC TGTTCCGACC CTGCCGCTTA

4600 4610 4620 4630 4640 4650 4660  
\* \* \* \* \*  
CCGGATACCT GTCCGCCTTT CTCCCTTCGG GAAGCGTGCC GCTTTCTCAA TGCTCACGCT GTAGGTATCT

4670 4680 4690 4700 4710 4720 4730  
\* \* \* \* \*  
CAGTTCGGTG TAGGTCGTT GCTCCAAGCT GGGCTGTGTG CACGAACCCC CCGTTCAGCC CGACCGCTGC

4740 4750 4760 4770 4780 4790 4800  
\* \* \* \* \*  
GCCTTATCCG GTAACATCG TCTTGAGTCC AACCCGGTAA GACACGACTT ATCGCCACTG GCAGCAGCCA

FIGURE 1E

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099324.1.130.1

|            |            |            |            |            |            |             |
|------------|------------|------------|------------|------------|------------|-------------|
| 4810       | 4820       | 4830       | 4840       | 4850       | 4860       | 4870        |
| CTGGTAACAG | GATTAGCAGA | GCGAGGTATG | TAGGCGGTGC | TACAGAGTTC | TTGAAGTGGT | GGCCTAACTA  |
| 4880       | 4890       | 4900       | 4910       | 4920       | 4930       | 4940        |
| CGGCTACACT | AGAAGGACAG | TATTTGGTAT | CTGCGCTCTG | CTGAAGCCAG | TTACCTTCGG | AAAAAGAGTT  |
| 4950       | 4960       | 4970       | 4980       | 4990       | 5000       | 5010        |
| GGTAGCTCTT | GATCCGGCAA | ACAAACCACC | GCTGGTAGCG | GTGGTTTTTT | TGTTTGCAAG | CAGCAGATTA  |
| 5020       | 5030       | 5040       | 5050       | 5060       | 5070       | 5080        |
| CGCGCAGAAA | AAAAGGATCT | CAAGAAGATC | CTTGATCTT  | TTCTACGGGG | TCTGACGCTC | AGTGGAAACGA |
| 5090       | 5100       | 5110       | 5120       | 5130       | 5140       | 5150        |
| AAACTCACGT | TAAGGGATTT | TGGTCATGAG | ATTATCAAAA | AGGATCTTCA | CCTAGATCCT | TTTAAATTAA  |
| 5160       | 5170       | 5180       | 5190       | 5200       | 5210       | 5220        |
| AAATGAAGTT | TTAAATCAAT | CTAAAGTATA | TATGAGTAAA | CTTGGTCTGA | CAGTTACCAA | TGCTTAATCA  |
| 5230       | 5240       | 5250       | 5260       | 5270       | 5280       | 5290        |
| GTGAGGCACC | TATCTCAGCG | ATCTGTCTAT | TTCTGTCATC | CATAGTTGCC | TGACTCCCCG | TCGTGTAGAT  |
| 5300       | 5310       | 5320       | 5330       | 5340       | 5350       | 5360        |
| AACTACGATA | CGGGAGGGCT | TACCATCTGG | CCCCAGTGCT | GCAATGATAC | CGCGAGACCC | ACGCTCACC   |
| 5370       | 5380       | 5390       | 5400       | 5410       | 5420       | 5430        |
| GCTCCAGATT | TATCAGCAAT | AAACCAGCCA | GCCGGAAGGG | CCGAGCGCAG | AAGTGGTCCT | GCAACTTTAT  |
| 5440       | 5450       | 5460       | 5470       | 5480       | 5490       | 5500        |
| CCGCCTCCAT | CCAGTCTATT | AATTGTTGCC | GGGAAGCTAG | AGTAAGTAGT | TCGCCAGTTA | ATAGTTTGCG  |
| 5510       | 5520       | 5530       | 5540       | 5550       | 5560       | 5570        |
| CAACGTTGTT | GCCATTGCTA | CAGGCATCGT | GGTGTCACGC | TCGTCGTTTG | GTATGGCTTC | ATTCAGCTCC  |
| 5580       | 5590       | 5600       | 5610       | 5620       | 5630       | 5640        |
| GGTCCCCAAC | GATCAAGGCG | AGTTACATGA | TCCCCCATGT | TGTGCAAAAA | AGCGGTTAGC | TCCTTCGGTC  |
| 5650       | 5660       | 5670       | 5680       | 5690       | 5700       | 5710        |
| CTCCGATCGT | TGTCAGAAGT | AAGTTGGCCG | CAGTGTTATC | ACTCATGGTT | ATGGCAGCAC | TGCATAATTC  |
| 5720       | 5730       | 5740       | 5750       | 5760       | 5770       | 5780        |
| TCTTACTGTC | ATGCCATCCG | TAAGATGCTT | TTCTGTGACT | GGTGAGTACT | CAACCAAGTC | ATTCTGAGAA  |
| 5790       | 5800       | 5810       | 5820       | 5830       | 5840       | 5850        |
| TAGTGTATGC | GGCGACCGAG | TTGCTCTTGC | CCGGCGTCAA | TACGGGATAA | TACCGCGCCA | CATAGCAGAA  |
| 5860       | 5870       | 5880       | 5890       | 5900       | 5910       | 5920        |

FIGURE 1F

CTTTAAAAGT GCTCATCATT GGAAAACGTT CTTGCGGGCG AAAACTCTCA AGGATCTTAC CGCTGTTGAG  
 5930 5940 5950 5960 5970 5980 5990  
 \* \* \* \* \*  
 ATCCAGTTCG ATGTAACCCA CTCGTGCACC CAACTGATCT TCAGCATCTT TTACTTTCAC CAGCGTTTCT  
 6000 6010 6020 6030 6040 6050 6060  
 \* \* \* \* \*  
 GGGTGAGCAA AAACAGGAAG GCAAAATGCC GCAAAAAAGG GAATAAGGGC GACACGGAAA TGTTGAATAC  
 6070 6080 6090 6100 6110 6120 6130  
 \* \* \* \* \*  
 TCATACTCTT CCTTTTTCAA TATTATTGAA GCATTTATCA GGGTTATTGT CTCATGAGCG GATACATATT  
 6140 6150 6160 6170 6180 6190 6200  
 \* \* \* \* \*  
 TGAATGTATT TAGAAAAATA AACAAATAGG GGTTCGCGC ACATTTCCCC GAAAAGTGCC ACCTGACGTC

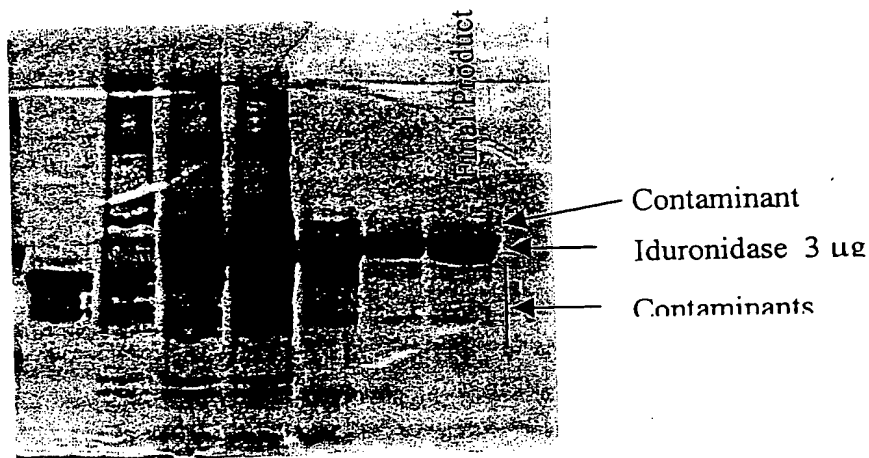
099341-11304

FIGURE 1G

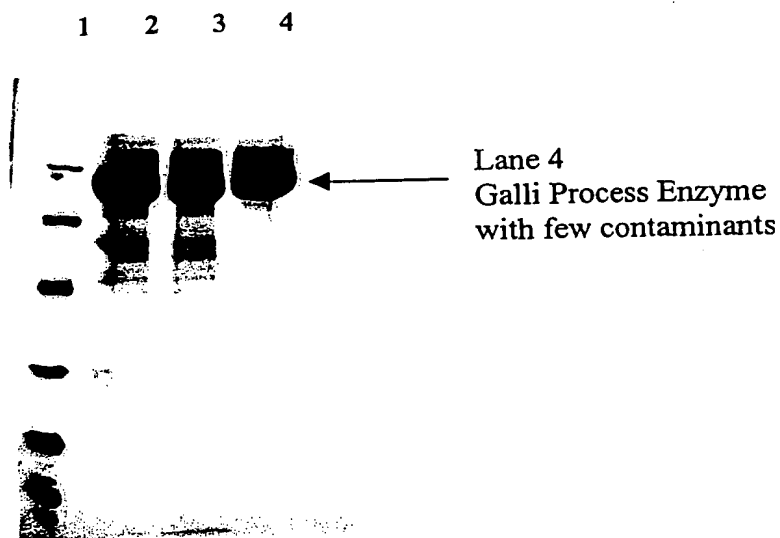


## FIGURE 2. SDS-POLYACRYLAMIDE GELS DEMONSTRATING IMPROVEMENTS IN PURITY

Gel using the Kakkis et al 1994, published procedure for purification



Gel using the new Galli Process contained in this application

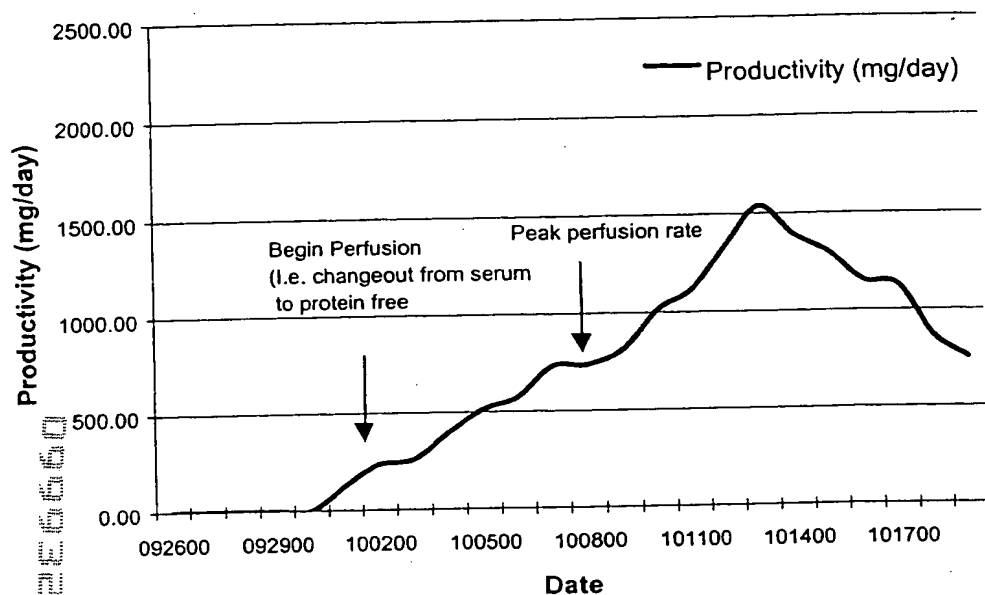


1. Molecular Weight Marker
2. Prior Process Carson (nonpublished) Batch 2000C9001 Reference Reduced (7.5  $\mu$ g)
3. Same Batch 2000C9001 Reference Reduced (5.0  $\mu$ g)
4. Galli Process Enzyme Batch P10006 (5.0  $\mu$ g)

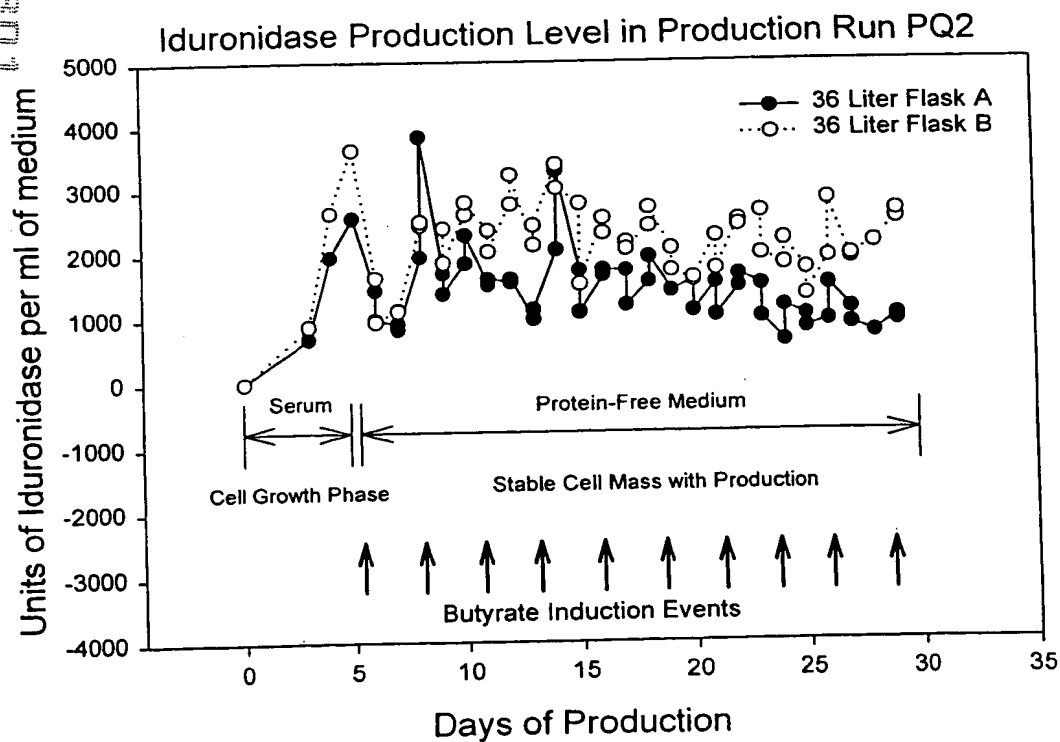
FIGURE 2

**FIGURE 3A IDURONIDASE PRODUCTION USING THE GALLI PROCESS**

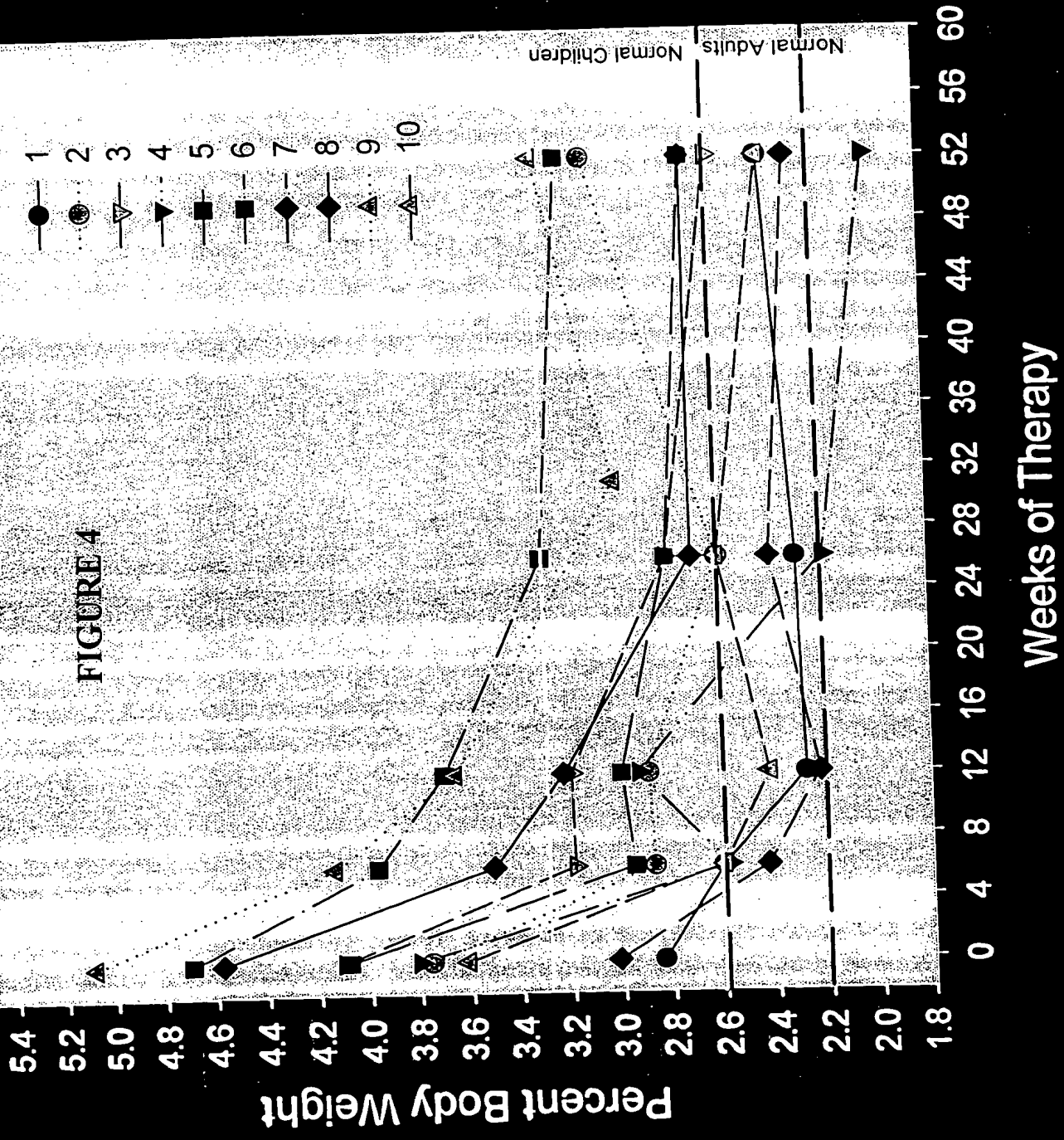
**Iduronidase Enzyme Activity During Production**



**FIGURE 3B. IDURONIDASE PRODUCTION USING BUTYRATE INDUCTION**



# Reduction in Liver Volume During Enzyme Therapy



**FIGURE 4**

# Urinary GAG Excretion During Enzyme Therapy

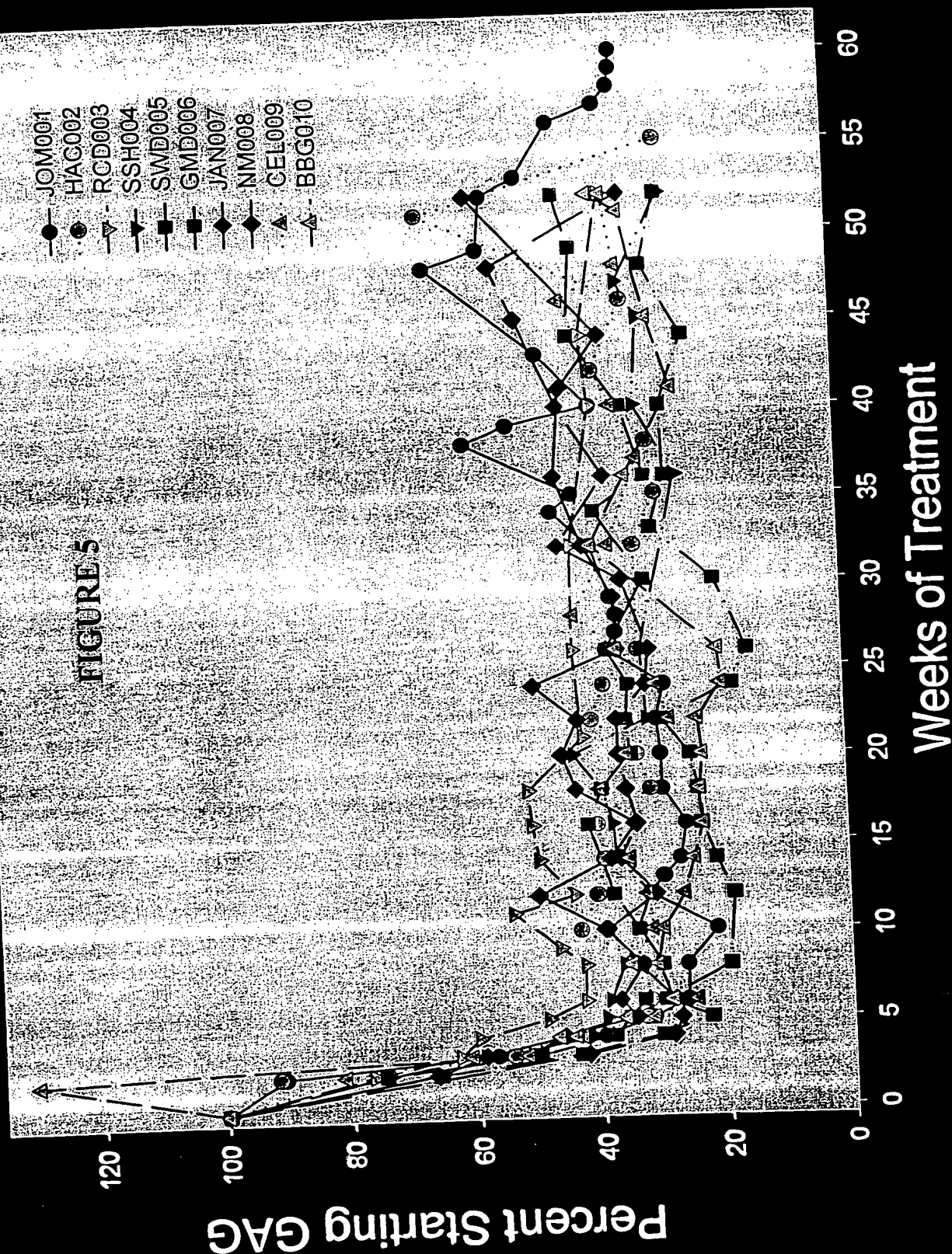


FIGURE 5

# Elbow and Knee Extension in HAC002

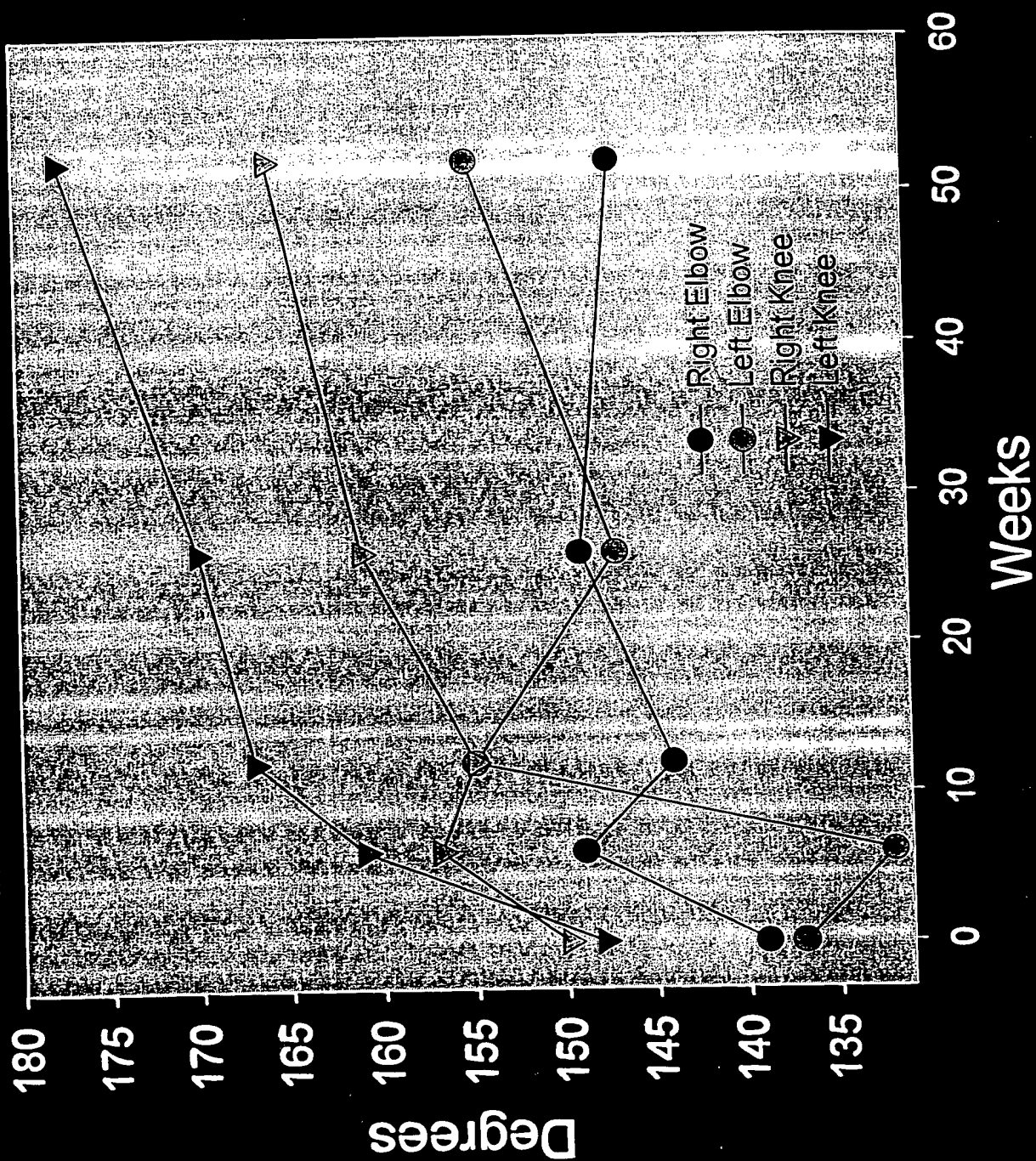


FIGURE 6

# Shoulder flexion to 104 weeks in four patients with most restriction

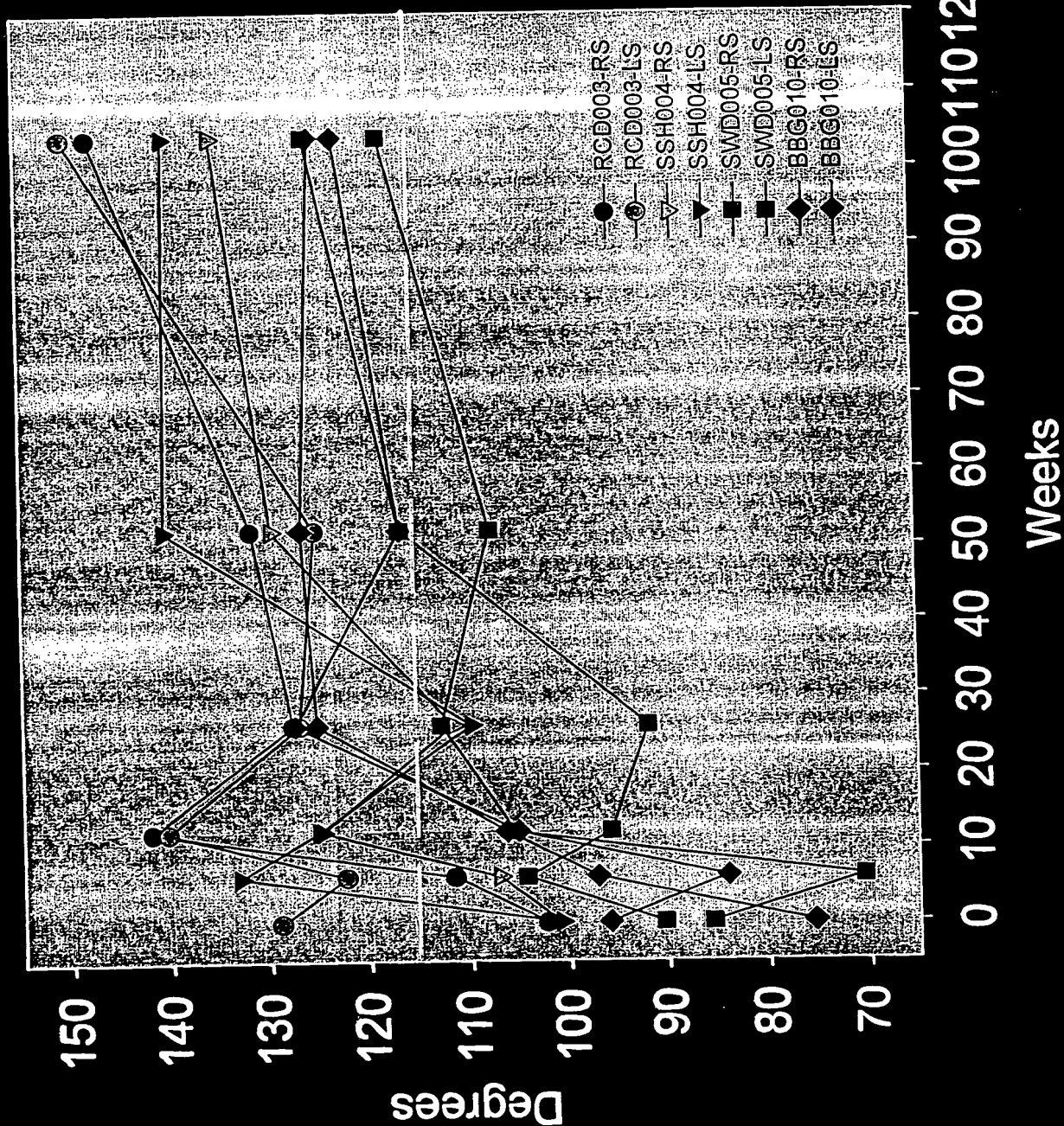


FIGURE 7

# Sleep Apnea Improves

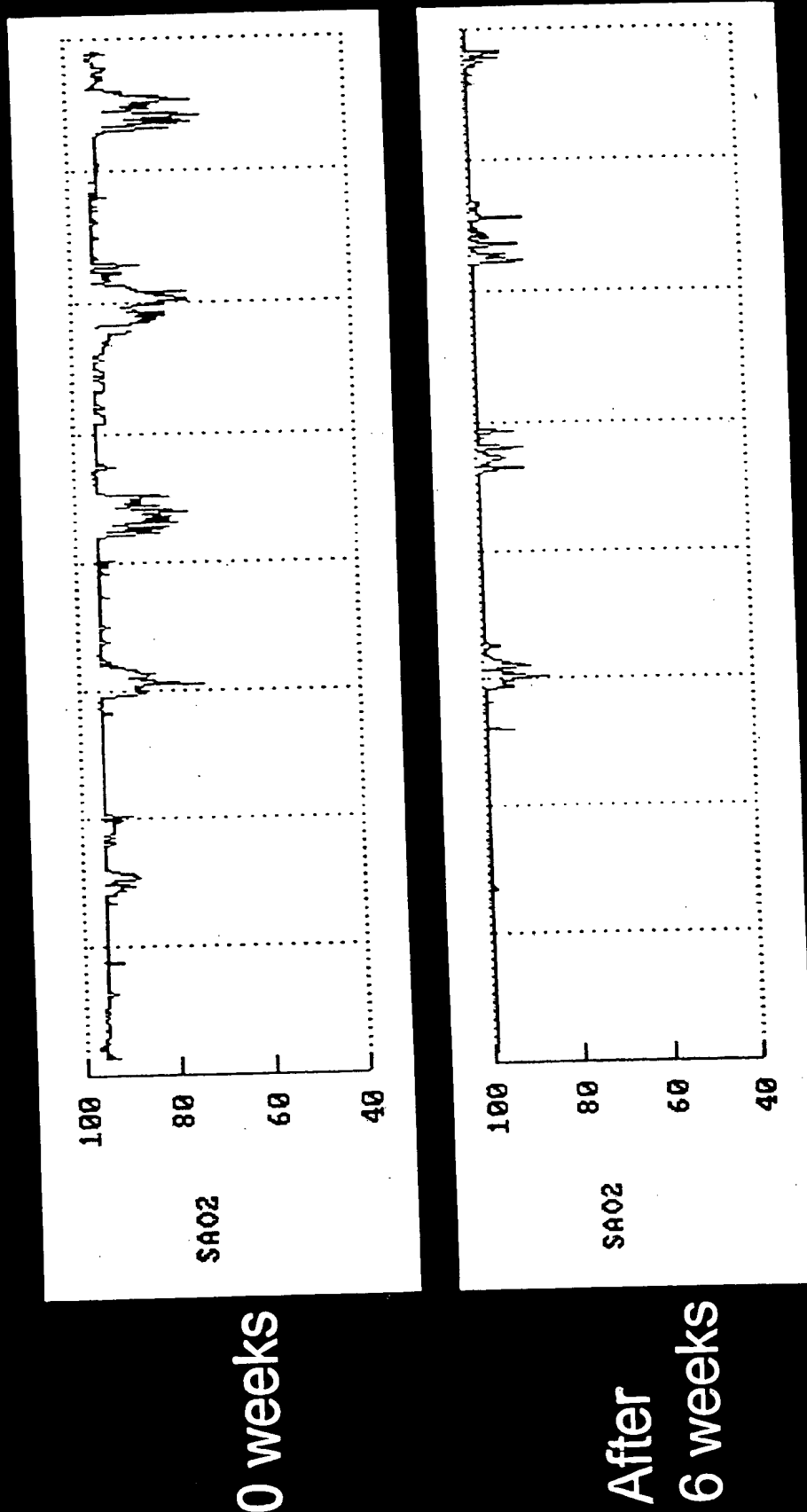
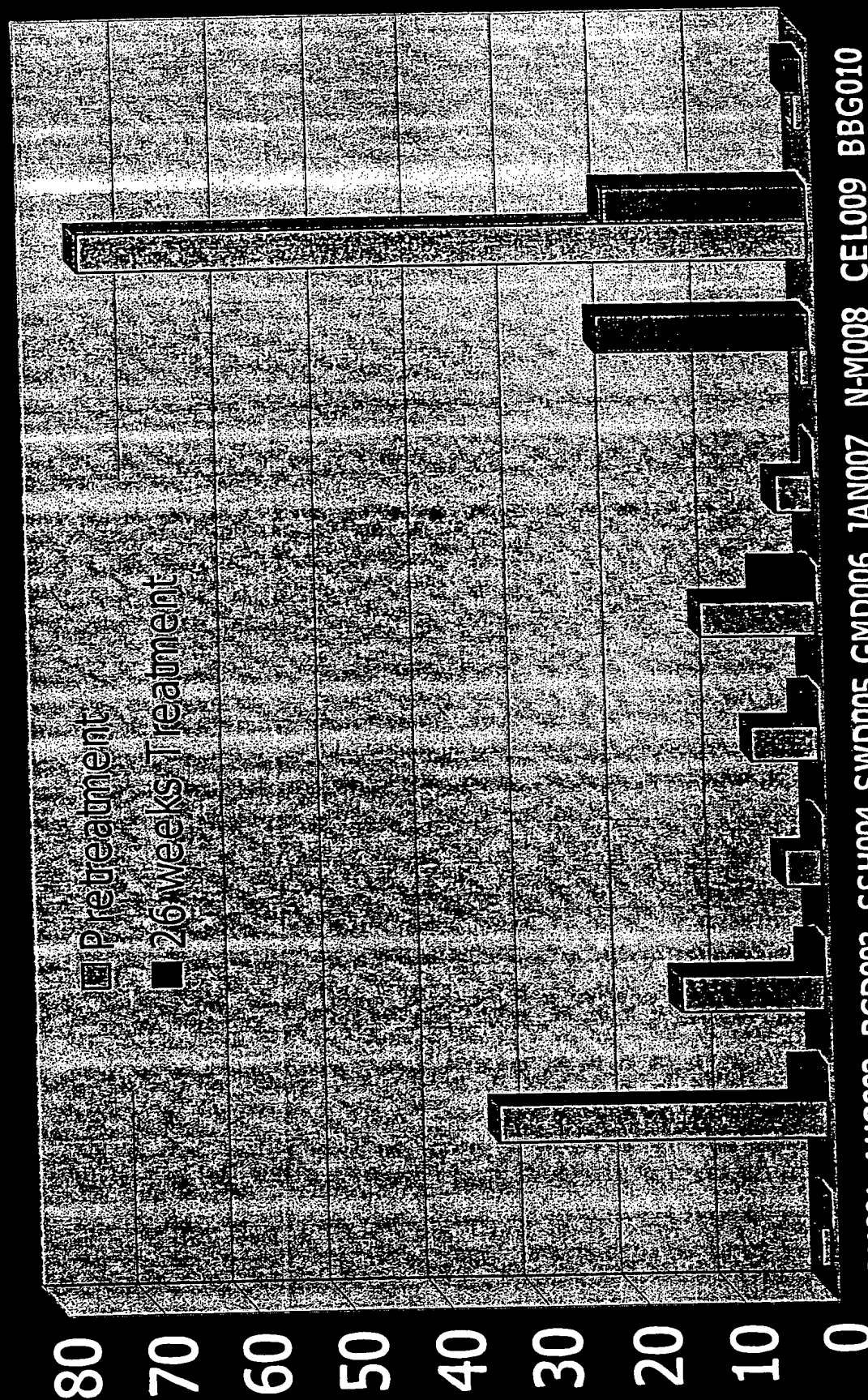


FIGURE 8



# Apneas + Hypopneas During Sleep

## Pre and Post Treatment



JOM001 AHC002 RCD003 SSH004 SWD005 GMD006 JAN007 N-M008 CEL009 BBG010

FIGURE 9



# Pulmonary Function Tests in GMD006

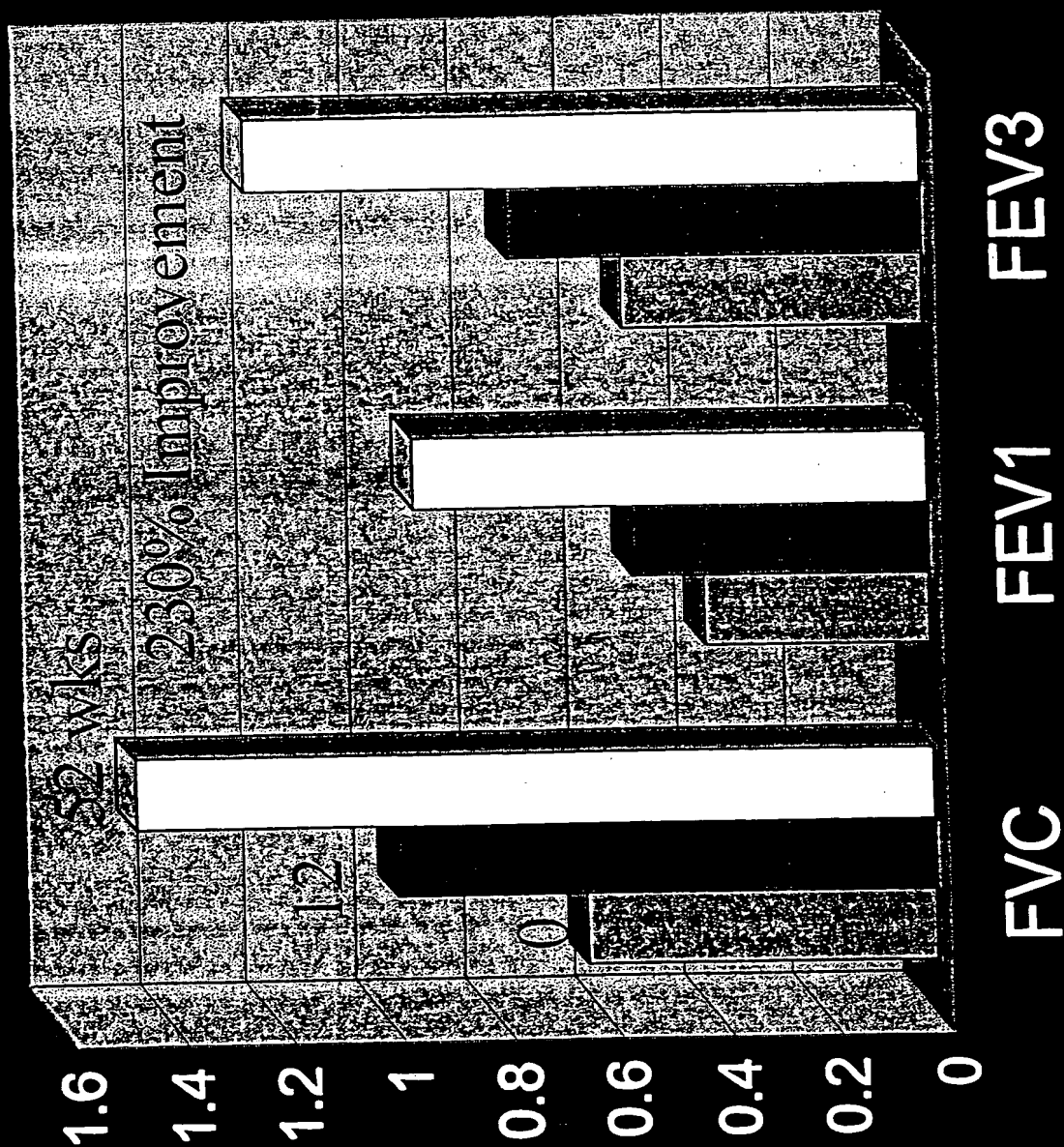


FIGURE 10

# Increased Height Growth Velocity

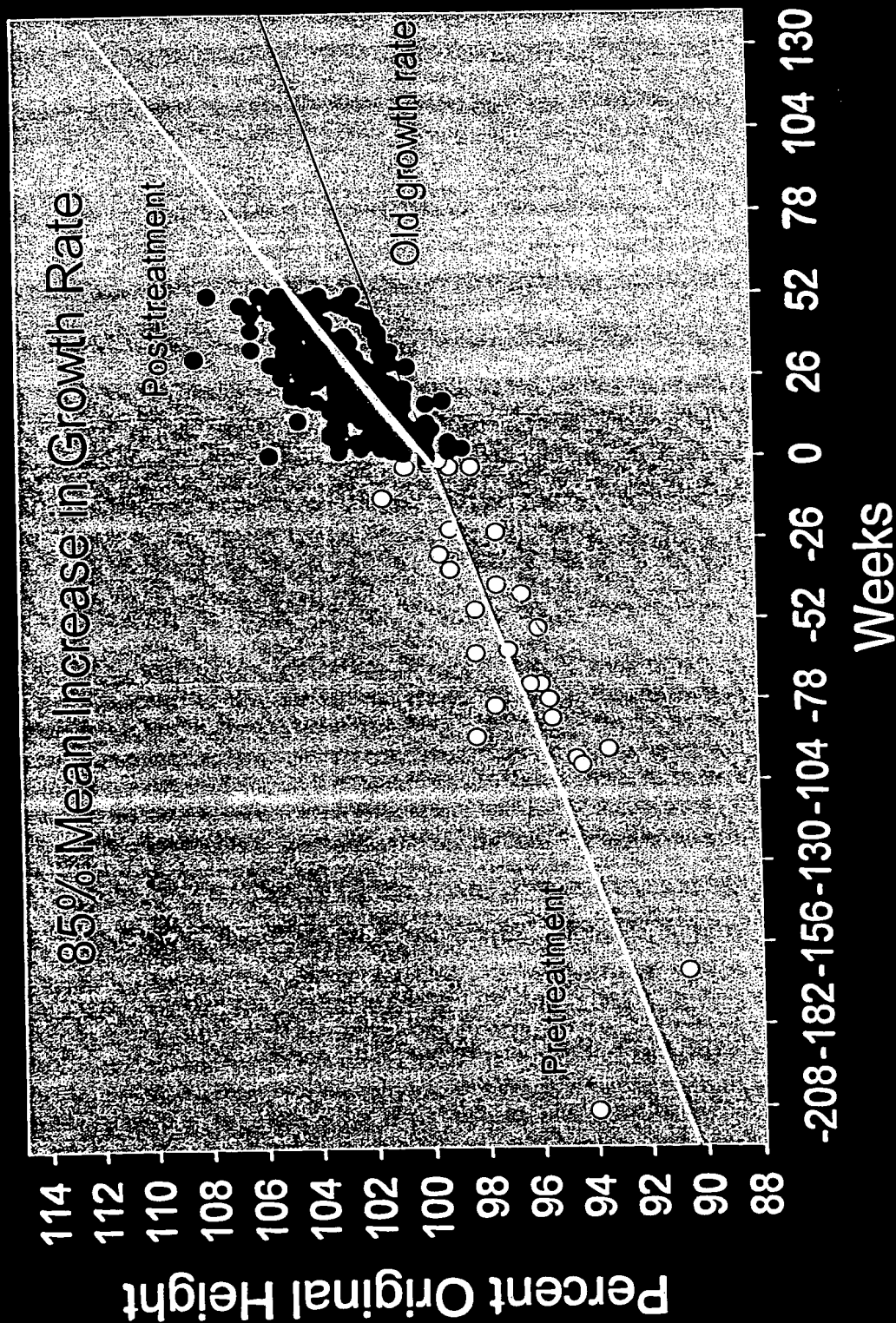


FIGURE 11

**FIGURE 12.**

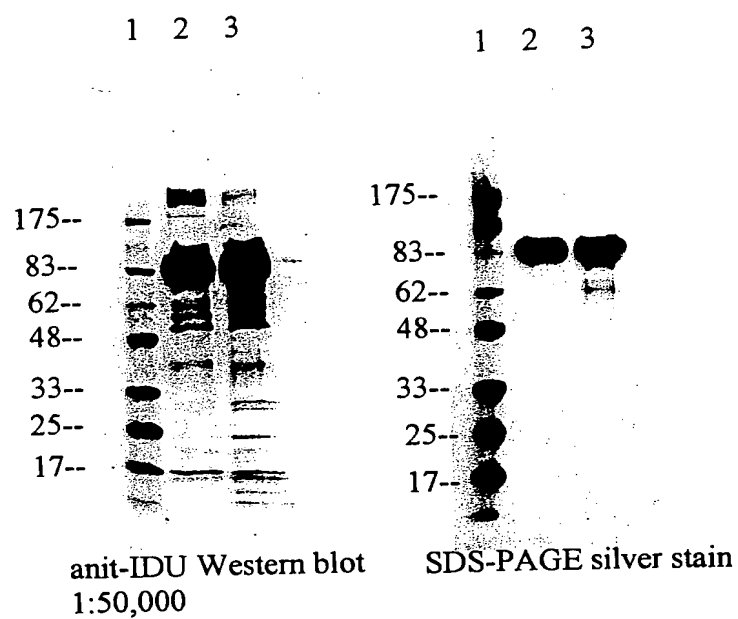
**COMPARISON OF HOST PROTEIN CONTAMINATION BETWEEN A PRIOR AND THE NEW GALLI PROCESS**

**Chinese Hamster Ovary Host Protein Contamination by ELISA Assay**

| SOURCE AND BATCH<br>NUMBER | CHOP PROTEIN<br>CONTAMINATION<br>(microgram per milligram) | PERCENT CHOP<br>CONTAMINATION | PURITY OF THE<br>ENZYME FROM<br>CHOP |
|----------------------------|--|-------------------------------|--------------------------------------|
| Prior Process (Carson/REI) |  |                               |                                      |
| C9002                      | 14   | 1.4%                          | 98.6%                                |
| C9003                      | 24   | 2.4%                          | 97.6%                                |
| C9004                      | 16   | 1.6%                          | 98.4%                                |
| New Process (Galli)        |  |                               |                                      |
| P1003                      | <1.3   | <0.13%                        | >99.9%                               |
| P1006                      | 1.2  | 0.12%                         | 99.9%                                |
| P1007                      | <0.6   | <0.06%                        | >99.9%                               |
| P1008                      | <0.67  | <0.067%                       | >99.9%                               |

**FIGURE 12**

# Comparison of Galli and Carson Material



1 Marker  
2 Galli Referenced-0201  
3 Carson C9002

5ug/lane

FIGURE 13